Figure 1

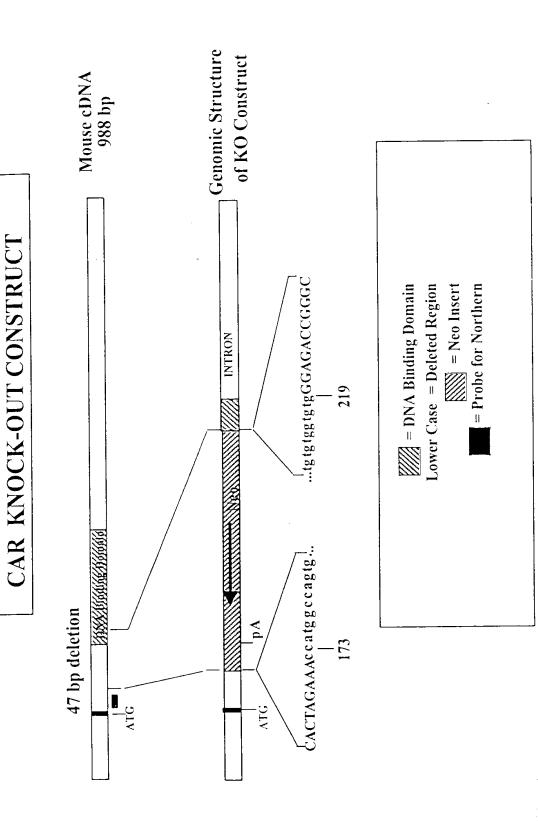


FIGURE 2

Section A.

.....aaaatttacccaacatagatttatctaatgtaattcctatctgcagaacatccaaatactttggaaattatttnttgtggttgtagctgtttgaatauttattagaatauttagaatagaatauttagaatauttagaatagaatauttagaatagaatagaatagaatauttagaagg cag tgg tgg cacacacctt ta atcccag cacttgg gag gcag ag gcag tgg a attatgag ttt gag gccag cct gg tctacag ag tgg and the sum of thtgtgatgtttatcacaatagaaagc.....

Section B. \dots aaagaggtcatcaggcttggcagcaagtgcctttgcctaccgagtctttacaccagctccaccgtggtttttgagacagtctccactgg actgg at ttcagca agaa agctagg ctt gccttctt gtctct gcctcctt gg cattgg aat tatgagt tgtccaccgt gccatttttaa aa aatgtagg ag tatgag ag tatgaggttctaggaattaaactcggctctcggtgcttatatagtgagtactttacagagggagtcaccttgccagcacctagaattcacttttattcatatct caga agge a agage te ctt ge ag aggatt ta acctea attect ag ta ctea actt ge cage te at a act ge cta ta acte ta green again to the contract of the contractctctcccattgtttcctggcttattcaggatccatgcaaaaaggggagtgtagatttagcctaaagctcacccacagggaaatcctccaggagt $\verb|ccccaccccacacccacacccagg| tettgccctgggtccagagtctgggtcctacctacatatggcaccgaggatacctagaggccccat|$ gaagagagteetatggeeeagtgetgatteteaacteeteeeacatteaggagaeeATGACAGCTATGCTAACACTAG<u>GGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGAGGGCTGCAAGGGCTTCTTCA</u> $\underline{Gg} tga atgette et cecea acaga a acceega cattte tate agtee accett ta aa caetgg ta caectee aa gt ta ta at cetett geagant to be a constant of the constant to the constant acceptance of the constant to the$ cta a get gea et gecea g t g teta gea et et ca a tet t get gacea ea a egea g t gaa a et g g t gacea a a g gea g g t ta a ceat g g t gacea et g g t g a ceat g g g t g a ceat g g g t g a ceat g g a ceat g g a ceat g g a ceat g g g a ceat g g g a ceat g a ceat g a ceat g a ceat g g a ceat gttgtcccagagacagagcctaagagtcaagaacacttgtgtagcacacactacctgcaaagcaccgagatgattgccacacgagggttcct $gagtaacettgtgtteteatgaaaaegeteeaactaeetetgaagaeetttgageaeageteagatgagtetgttgttaaategatee\ldots \\$

Section C.

.....t g cattgett teta et gaag t gaat a tagag at eaga a tagag a tagag a tagag ga te ee et gee a teta gaat a tagag a tagag a tagag ga te ee et gee a tagag aca at gaag tee caaggaag cete agaa actett teet teet teet teet teet ta tet ggg gagg t gg ag t gg ee caa et gaaggg at gg et gaaggaag teet agaaggaag get gaggaag teet agaaggg at gg ee gaggaag teet agaaggg at gg ee gaggaag teet agaaggg at gg ee gaggaag teet gaaggaag teet agaaggg at gg ee gaggaag teet agaaggg at gg ee gaggaag teet agaaggg at gg ee gaggaag teet agaag teet agaaga caggea cag egge egge agaa agaa et et t t gea act gaat cag eagaa agaa et g g t cag at cet cet egg g g e cea cact en act gea en act gea et en act gea et en act gea en act gea en act gea et en act gea et en act gea en actaagaaggctatgccctgatggaggaca

5g-Pregnan-3,20-dione is an hCAR Agonist

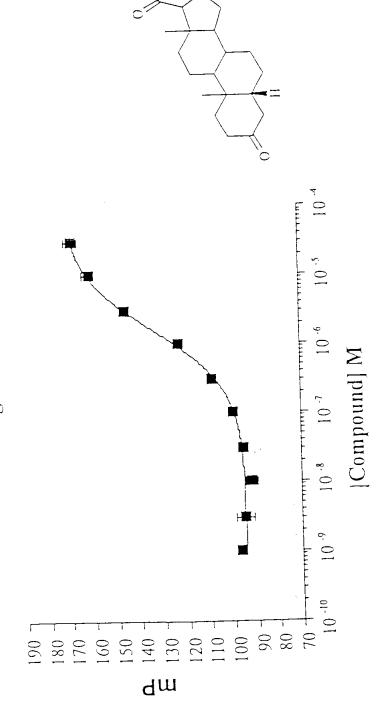
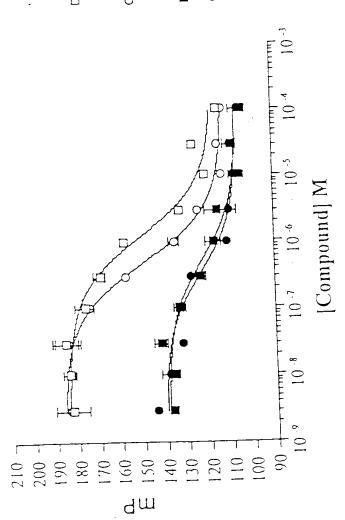


Figure 3

Androstanes are hCAR Antagonists



$$_{\rm S}$$
 $_{\rm C}$ $_{\rm Androst-16-en-3}$ $_{\rm C}$ $_{\rm C$

1.2 µM

IC 50

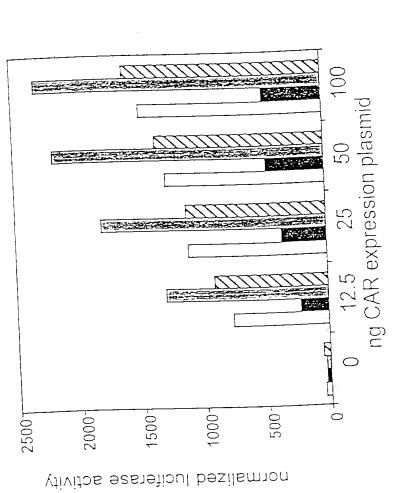
$$5\,\alpha$$
-Androstan-3 α -ol + $5\,\mu M$ 5 β -Pregnan-3,20-dione

480 nM

$$5\alpha$$
-Androst-16-en-3 α -ol 5α -Androstan-3 α -ol

$$5\alpha$$
-Androstan- 3α -ol

$$5\alpha$$
-Androst-16-en- 3α -ol

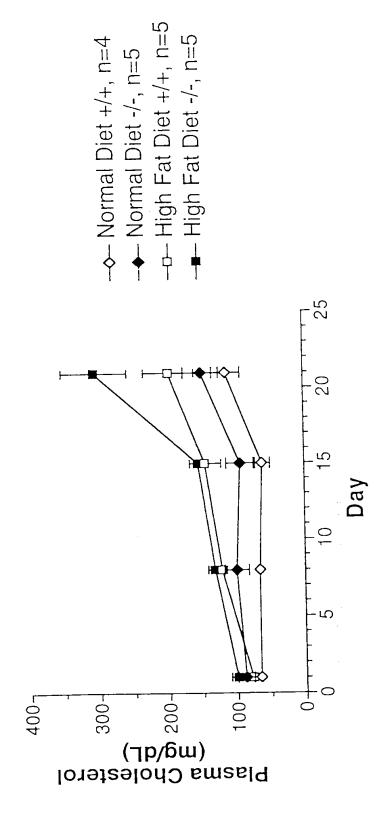


🛘 vehicle

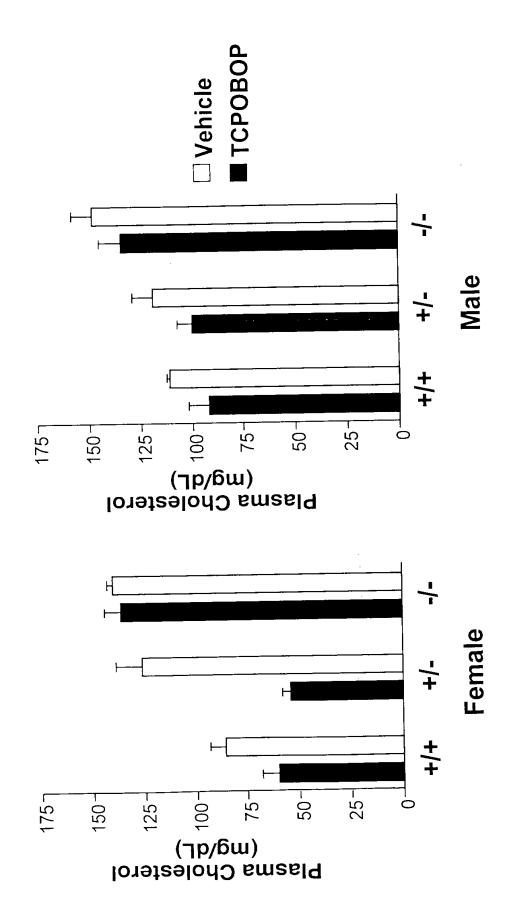
■ 5α-androstan-3α-ol

₪ 5β-pregnan-3,20-dione

 α 5 α -androstan-3 α -ol + 5 β - pregnan-3,20-dione



High Fat diet = Picolab 5053 (containing 1.25% cholesterol and 10% fat) Normal diet = Picolab 5053 (containing 4% fat)





F F WT WT

т <u>Х</u>

≥ &

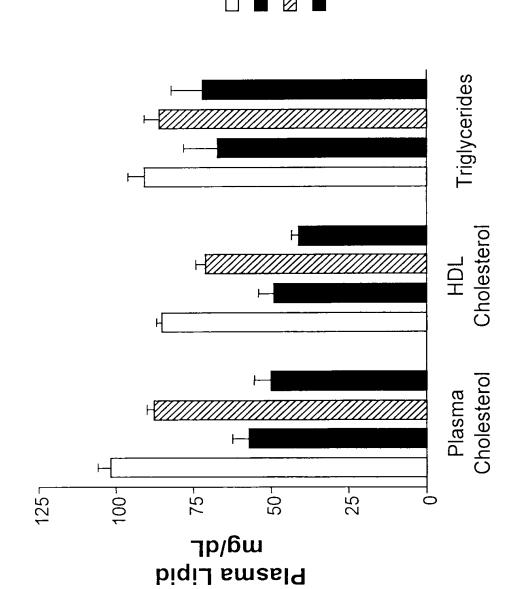
∑×

SEX GENOTYPE

- LDL/VLDL] HDL *** TCPOBOP Treated

F F WT WT тХ О ≥ ♀ $\mathbb{Z} \overset{\vdash}{\otimes}$ $\mathbb{Z} \stackrel{\vdash}{\geqslant}$ SEX GENOTYPE

- Origin



Male - Vehicle
Male - TCPOBOP
Female - Vehicle
Female - TCPOBOP